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Dyes Derived from Aminothiophenes. Part 1: Synthesis of Some Heterocyclic Disperse Dyes using the Gewald Reaction

Geoffrey Hallas & Andrew D. Towns

Department of Colour Chemistry and Dyeing, University of Leeds, Leeds LS2 9JT, UK

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ABSTRACT

A series of red to violet thienyl-2-azo disperse dyes has been derived from aminothiophenes synthesised directly by using the Gewald reaction. A variety of diazotisation conditions had to be employed owing to the differing basicities, hydrophobicities and stabilities of each thiophenamine. ^{13}C *NMR data for certain derivatives are reported. Copyright © 1996 Elsevier Science Ltd*

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1. INTRODUCTION

The development by Gewald in the 1960s of a simple and versatile synthetic method for 2-aminothiophenes, as part of his research into the preparation of heterocycles from active-methylene nitriles,[1,2] sparked renewed commercial interest in these compounds as diazo components. The earlier work of Dickey *et al.*[3] had established the potential of thienylazo disperse dyes, although their use was frustrated by the unfavourable economics of the available chemistry.[4] The promise of Gewald's discovery signalled a burst of patent activity,[5,6] which was followed by a steady stream of applications concerning thiophene-based azo disperse dyes over the next 20 years.[7,8] Despite, or perhaps because of, the commercial interest, few papers have been published concerning the synthesis and properties of such dyes.

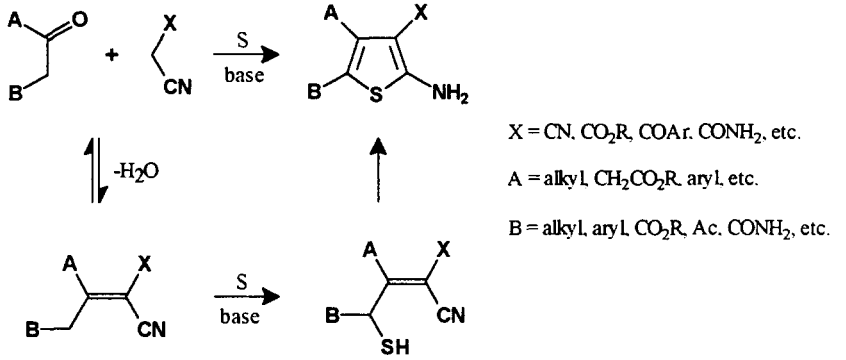
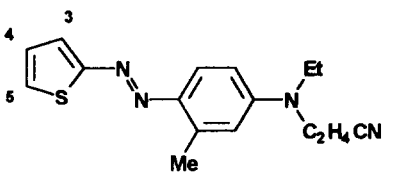


Fig. 1. Aminothiophenes from carbonyl compounds, active α-methylene nitriles and sulphur.

The original version of Gewald's synthesis involved the reaction of α-carbonylthiols with nitriles possessing an active α-methylene group, in the presence of catalytic amounts of base.[9,10] A range of electron-withdrawing substituents can be introduced into the 3-position, but the choice of substituents in the 4- and 5-positions is limited by the accessibility of the required α-carbonylthiols. Subsequently, a broader method for the preparation of selected thiophenamines was described[11,12] which utilised carbonyl compounds having an active α-methylene function, in the presence of elementary sulphur and base (see Fig. 1).

This method is less restricted than the original in that the structure of the carbonyl compound can be varied to give a wider range of 4- and 5-substituents; for example, cyclic ketones give 4,5-alkylene substitution, while alkyl acetoacetates yield a 5-alkyloxycarbonyl-4-methyl pattern. Enamines can be used in place of the carbonyl component,[13] for example, 3-aminocrotononitrile to introduce 5-cyano-4-methyl substitution.[14,15] For a one-stage reaction, the carbonyl and methylene groups must be sufficiently reactive to undergo a Knoevenagel condensation to form an intermediate *in situ*, which then cyclises irreversibly, otherwise an ylidene intermediate has to be preformed in a first stage and then cyclised in a discrete second stage,[11,12] as is the case for acetophenone-based compounds.[16]

This paper details the preparation of dyes **1** by conventional methods from



thiophenamines obtained directly via variations of the Gewald synthesis shown in Fig. 1.

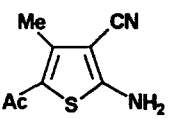
2. RESULTS AND DISCUSSION

2.1. Preparation of the diazo components

While the 2-amino-3-alkoxycarbonyl-(4,)5-alkyl(ene)thiophenes can be prepared without difficulty in a 'one-pot' reaction, the 2-amino-3-cyano-4,5-alkylenethiophenes were better prepared via the two-stage rather than the one-stage method. The added complication of two steps was justified by almost quantitative crude yields of high purity. The 4,5-dimethyl analogue was prepared by the two-stage method because of the known complications caused by malononitrile–butanone interactions interfering with thiophene formation.[1] In the synthesis of 2-amino-3-cyanothiophenes from the isomeric tetralones, tetral-2-one was amenable to direct synthesis, whereas tetral-1-one was sufficiently deactivated towards reaction with malononitrile, because of the close proximity of the aromatic ring to the carbonyl group, to warrant a separate condensation step.

When aldehydes were used as the carbonyl components, the special conditions recommended by Gewald *et al.*[12] were applied. The presence of these compounds with base creates a potential for reactions which compete with thiophene formation, such as aldol condensation. The aldehyde concentration, therefore, must be kept as low as possible to avoid self-reaction; the aldehyde was added at such a rate to the mixture of nitrile, sulphur and base in DMF (a polar solvent to promote a fast reaction) so as to prevent adverse build-up of aldehyde concentration.

The one-stage syntheses using β-dicarbonyl compounds involved heating to relatively high temperatures (60–75°C) to obtain satisfactory yields as outlined by Gewald *et al.*[12] and Wierzbicki *et al.*[17] An exception was the attempted synthesis of **2**.



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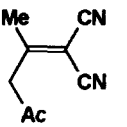

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Addition of the catalyst (morpholine, 5 ml) to the mixture of starting materials (0.10 mol) in ethanol (20 ml) at 40°C, as in the normal method,

initiated a rapid exothermic reaction; material precipitated, the ethanol boiled and most of the reaction mixture was lost in a mild explosion. Use of external cooling (ice-water), gradual addition of catalyst (over 10 min) and double the amount of solvent pacified the reaction, although precipitation of material was still rapid. Stirring for 1 h at 60°C, filtering and water-washing gave 8.00 g of an off-white solid (m.p. >280°C), which was recrystallised repeatedly from ethanol/DMF (2:1) to furnish white needle-like crystals [m.p. 291–292°C (dec.), DSC showed a sharp endotherm at 289.1°C]. Analysis revealed that the product was not a thiophene, but the intermediate condensation compound **3**: FTIR (KBr)/cm^{-1} 2219 (C≡N), 1657 (C=O); ^1H NMR 2.18, 2.26 (3H, s, CH_3), 6.10 (2H, s, CH_2); microanalysis found, C, 65.1; H, 5.5; N, 19.3% ($C_8H_8N_2O$ requires C, 64.8; H, 5.4; N, 18.9%). Further attempts at the synthesis of **2** from the one-step method or by cyclisation of **3** with sulphur were not pursued.

Derivatisation of 2-amino-3-ethoxycarbonyl-4,5-tetramethylenethiophene was undertaken. Transesterification by the refluxing of an ester in an excess of the alcohol corresponding to the target ester with titanium isopropoxide under nitrogen[18] is useful because of the mild conditions involved. Attempted conversions of the ethyl ester into the isopropyl and *n*-propyl forms were unsuccessful. Use of *N*-acetylated starting material was made in the hope that the reduced interaction of the amino nitrogen lone pair with the ester carbonyl group would be favourable, but without success. No problems were encountered with transesterification to the *n*-butyl ester for either the free amine or the *N*-acetyl derivative. The success of the butyl ester synthesis may be related to the higher boiling point of the solvent and consequent reflux temperature. (The propyl esters were prepared from the corresponding cyanoacetates instead.)

2.2. Preparation of the dyes

The diazo components used in this study possessed a wide range of basicities. Thiophenes with only one moderately electron-withdrawing group could, with a few exceptions, be diazotised in dilute mineral acid. The 3-cyano-4,5-alkylene derivatives were diazotised in 35% aqueous sulphuric acid. The method represented an improvement on that of Sabnis and Rangnekar[19] who used 17% aqueous HCl. For example, whilst crude yields were similar (79% and 80%, respectively), the purity of the product was higher in the former method for the 4,5-tetramethylene derivative.[20] A greater acid concentration (54%) was required with increases in hydrophobicity through enlargement of the size of the alkylene ring or by the fusion of an aromatic ring.

The 3-alkoxycarbonyl-4,5-alkylenethiophenes proved to be more problematical. The methyl and ethyl esters were diazotised in 17% aqueous HCl

after Sabnis and Rangnekar[19] in reasonable yield, but the degree of purity was disappointing. Other attempts with 35% aqueous sulphuric acid/sodium nitrite and with nitrosylsulphuric acid proved too destructive and gave products with negligible dye content. The higher esters were too hydrophobic for 17% aqueous HCl; addition of solvent such as acetone to aid solubility did give a very impure product, but further synthesis of the three relevant dyes was not pursued. The 4,5-pentamethylene analogues required additional solubilisation and the 4,5-trimethylene analogues, as well as the 3-methoxycarbonyl-4,5-dimethyl derivative, decomposed visibly so that a method[21] involving a shortened diazotisation time had to be used. The effect of small structural changes on diazotisation behaviour was further demonstrated with the 3-methoxycarbonyl-5-alkyl series, which could be diazotised satisfactorily with the 35% aqueous sulphuric acid/sodium nitrite system, unlike the closely related derivatives discussed above. The 5-phenyl analogue had an increased hydrophobicity so that even 54% aqueous sulphuric acid was not a satisfactory solvent, but the aryl group conferred enough stability to make diazotisation with nitrosylsulphuric acid viable, and this was the preferred method for thiophenamines possessing more than one electron-withdrawing group.

2.3. Physical properties of the dyes

When adsorbed onto silica or alumina chromatography plates, the dyes produced yellow–red to violet colours, for example (**1**; 3-CO_2R-4,5-alkylene) and (**1**; 3,5-CN-4-Me), respectively. The expected tendency of the more polar (and bathochromic) members of the dye series towards lower R_f values was observed. Other trends in the physical properties of the dyes could be identified.

2.3.1. Melting points

All the purified dyes exhibited well-defined melting points characteristic of pure compounds (see Table 1). Whilst it would be unwise to attempt to explain in detail their relative values, because of the complex dependence of the melting points on a number of factors, a few general trends can be accounted for.

The dyes prepared from low-melting diazo components tended to have low melting points themselves and the factors determining high melting points were preserved in the dyes from high-melting heterarylamines. Thienyl-2-azo dyes with 3-cyano groups had higher melting points than analogues with a 3-alkoxycarbonyl group, which may be a result of increased polarity and/or the rod-like shape of the cyano group being more conducive to efficient packing in the crystal structure. Replacement of the ester function with an

TABLE 1
Melting Points of some 3-Methoxycarbonyl- and 3-Carbamyl-thienyl-2-azo Dyes **1**

3	4	5	m.p. (°C)	Ref.
CO_2Me	$-(CH_2)_4-$		139–139.5	20
$CONH_2$	$-(CH_2)_4-$		215.5–216	20
CO_2Me	H	Ph	141.5–142	
$CONH_2$	H	Ph	189–189.5	

amido group provides an opportunity for increased intermolecular interaction through hydrogen-bonding and is reflected in the relatively high melting points of (**1**; 3-$CONH_2$-4,5-$(CH_2)_4$-) and (**1**; 3-$CONH_2$-5-Ph) compared to their 3-methoxycarbonyl analogues (see Table 1).

Increasing the chain length of the 5-alkyl substituent in the (**1**; 3-CO_2Me-5-R) series reduced the melting point (R = Me, 138.5–139°C; R = Et, 107–107.5°C; R = Bu, 76–76.5°C), presumably by making packing less efficient.

2.3.2. ^{13}C NMR analysis

The carbon-13 NMR spectra of some of the more structurally simple dyes were recorded; the data are listed in Table 2. There would appear to be no ^{13}C NMR data available in the literature for thienylazo dyes; however, the observed chemical shifts correlated well with those reported for a phenylazo toluidine-based analogue.[22]

3. EXPERIMENTAL

Chromatography was performed as previously described.[20] Melting points were determined using an Electrothermal melting point apparatus and were uncorrected. Thermal analysis was performed on a DuPont 2000 differential scanning calorimeter. Fourier-transform infra-red spectra were obtained with a Perkin-Elmer 1740 spectrophotometer in nujol mull or KBr discs. ^1H NMR and ^{13}C NMR spectra were recorded on a Jeol 200 MHz machine.

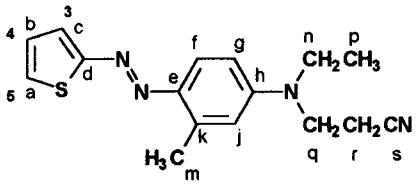
3.1. Preparation of intermediates

Research samples of 2-amino-3,5-dicyano-4-methylthiophene (YCL) and 5-acetyl-2-amino-3-methoxycarbonylthiophene (Department of Colour Chemistry) were acquired; the other aminothiophenes were obtained directly by the Gewald reaction, or through transesterification, as described below.

2-Amino-3-ethoxycarbonyl-4,5-trimethylenethiophene[11] and 2-amino-3-ethoxycarbonyl-4,5-pentamethylenethiophene[23] were prepared in a similar

TABLE 2

^{13}C NMR Data for a Phenylazo Dye and some Thienyl-2-azo Dyes in Chloroform



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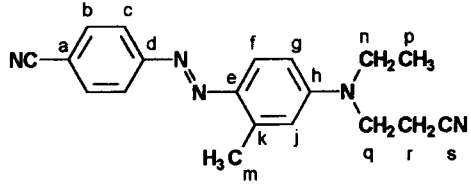

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Dye	Substituents	a	b	c	d	e	f	g	h	j	k	m	n	p	q	r	s	Misc.
1	3-CN-4,5-$(CH_2)_3$-	α	α	104.50	170.46	α	117.64	110.31	149.50	112.56	141.70	18.07	45.78	12.56	46.31	16.29	119.16	β
1	3-CO_2Me-4,5-$(CH_2)_3$-	χ	χ	χ	164.28	142.73	117.88	110.80	149.35	113.24	142.06	18.66	46.28	13.17	46.96	16.82	118.35	δ
1	3-CO_2Et-4,5-$(CH_2)_3$-	ε	ε	ε	163.20	142.18	117.76	110.17	148.68	112.62	141.44	18.05	45.67	12.56	46.34	16.21	118.91	φ
1	3-CO_2Et-4,5-$(CH_2)_4$-	γ	γ	γ	159.90	142.03	117.88	110.05	148.63	112.59	141.27	18.05	45.61	12.53	46.28	16.21	118.58	η
1	3,5-CN-4-Me	φ	κ	φ	171.19	145.44	117.35	110.87	κ	112.68	141.99	18.40	46.19	12.76	46.35	16.53	120.71	λ
4	—	110.84	133.56	122.53	155.22	142.54	117.23	110.35	150.71	112.54	141.31	—[a]	44.53	12.28	45.34	15.88	—[a]	Ref. 22

α 145.88, 142.78, 142.37; β (CN) 114.63, ((-CH_2)$_3$-) 30.22, 27.97, 27.56; χ 148.66, 124.71; δ (CO_2CH_3) 167.05, (CO_2CH_3) 52.26, ((-CH_2)$_3$-) 30.55, 28.06; ε 147.08, 124.54; φ ($CO_2CH_2CH_3$) 166.29, ($CO_2CH_2CH_3$) 60.47, ($CO_2CH_2CH_3$) 14.34, ((-CH_2)$_3$-) 29.90, 27.45; γ 137.27, 135.66, 129.36, η ($CO_2CH_2CH_3$) 164.13, ($CO_2CH_2CH_3$) 60.68, ($CO_2CH_2CH_3$) 14.46, ((-CH_2)$_4$-) 25.70, 25.23, 22.81, 22.34; φ 108.24, 103.71; κ 151.86, 149.88; λ (CN) 113.35, 113.06, (CH_3) 15.16.

[a]Values not given.

manner to their methyl ester analogues (see Sections 3.1.1 and 3.1.2, respectively). The 2-amino-3-alkoxycarbonyl-4,5-dimethylthiophenes[10,12] were synthesised in an analogous fashion to 3.1.1. The 3-cyano-4,5-alkyl(ene) derivatives were prepared in a similar manner to 2-amino-3-cyano-4,5-hexamethylenethiophene (see Section 3.1.7). 2-Amino-3-cyano-4,5-dihydrobenzo[*g*]-thianaphthene[24] and 2-amino-3-cyano-8,9-dihydrobenzo[*e*]thianaphthene[25] were prepared from tetral-2- and -1-one, respectively, by literature methods. The 5-ethyl[26] and 5-butyl[27] derivatives of 2-amino-3-carboxymethylthiophene were prepared by following the method used for the 5-methyl compound (see Section 3.1.8). The synthesis of 2-amino-3-carbamyl-5-phenylthiophene[12] was based on that of its 3-methoxycarbonyl analogue (see Section 3.1.9).

3.1.1. 2-Amino-3-methoxycarbonyl-4,5-trimethylenethiophene

Cyclopentanone (99%, 8.49 g, 0.10 mol), methyl cyanoacetate (99%, 10.01 g, 0.10 mol) and sulphur (3.21 g, 0.10 mol) in methanol (20 ml) were stirred and treated with diethylamine (10 ml) over 15 min, keeping the mixture temperature below 35°C (external water-cooling). A thick dark yellow suspension was obtained after stirring at 40–45°C for 3 h, and this was then stored overnight in a refrigerator. Filtering, washing with methanol and then water, followed by drying at 70°C gave a pale yellow powder (12.10 g, 61% crude yield). Four recrystallisations (2-ethoxyethanol) yielded a sandy-coloured crystalline solid (m.p. 180–181°C) of analytical purity. Microanalysis found C, 54.75; H, 5.75; N, 7.15; S, 16.25% ($C_9H_{11}NO_2S$ requires C, 54.8; H, 5.6; N, 7.1; S, 16.25%). DSC indicates purity, showing a sharp endotherm at 181.3°C. FTIR (KBr)/cm^{-1}: 3410, 3292 (NH); 1657 (C=O).

3.1.2. 2-Amino-3-methoxycarbonyl-4,5-pentamethylenethiophene

As for Section 3.1.1 except that the ketone used was cycloheptanone (97%, 11.56 g, 0.10 mol). The liquor was allowed to stand at room temperature for 3 days leading to the formation of large rod-like, yellow crystals which were filtered off and washed with ice-cold methanol (6.38 g, 38% crude yield, m.p. 93–94°C). Recrystallisation from methanol gave salmon-pink translucent needles (5.94 g, m.p. 93.5–94°C). Microanalysis found C, 58.45; H, 6.75; N, 6.2; S, 14.35% ($C_{11}H_{15}NO_2S$ requires C, 58.6; H, 6.7; N, 6.2; S, 14.2%). FTIR (KBr)/cm^{-1}: 3409, 3303 (NH); 1652 (C=O).

3.1.3. 2-Amino-3-propoxycarbonyl-4,5-tetramethylenethiophene

As for Section 3.1.1 except that propyl cyanoacetate (12.71 g, 0.10 mol, prepared by reaction of cyanoacetic acid and propan-1-ol catalysed by H_2SO_4, b.p. 217–219°C, lit.[28] 216°C) and ethanol (20 ml) were used in place of the methyl ester and methanol. After allowing to crystallise overnight, yellow–orange needles were filtered off, washed with ice-cold ethanol and then water

to give pale yellow needles (15.29 g, 64% crude yield, m.p. 81–82°C). Further solid was obtained by dilution of the filtrate to give a combined mass of 19.40 g (81% total crude yield). Recrystallisation (60–80° ligroin, ethanol) of the first crop furnished light beige, translucent crystals (14.25 g, m.p. 81.5–82°C) of analytical purity. Microanalysis found C, 60.1; H, 7.1; N, 6.0; S, 13.25% ($C_{12}H_{17}NO_2S$ requires C, 60.2; H, 7.2; N, 5.85; S, 13.4%). PMR (DMSO-d_6): 2.5–2.7 (4H, m, 4- and 7-CH_2), 1.75 (4H, m, 5- and 6-CH_2), 4.2 (2H, t, $CO_2CH_2CH_2$), 0.85–1.5 (5H, m, $CO_2CH_2CH_2CH_3$), 7.4 (2H, broad s, NH_2).

3.1.4. 2-Amino-3-isopropoxycarbonyl-4,5-tetramethylenethiophene

Diethylamine (5 ml) was added to a stirred mixture of isopropyl cyanoacetate (6.36 g, 0.05 mol), cyclohexanone (4.91 g, 0.05 mol), sulphur (1.60 g, 0.05 mol) and ethanol (7 ml) over 10 min so that the reaction temperature did not exceed 35°C. The mixture was stirred for 3 h at 40–45°C and then allowed to crystallise over 2 days. Water-washing and air-drying after filtration produced orange flakes (10.37 g, 87% crude yield). Two recrystallisations (100–120° ligroin) gave analytically pure, light beige crystals of m.p. 59–60°C. Microanalysis found C, 60.1; H, 7.1; N, 5.7; S, 13.3% ($C_{12}H_{17}NO_2S$ requires C, 60.2; H, 7.2; N, 5.9; S, 13.4%). PMR ($CDCl_3$): 2.5–2.8 (4H, m, 4- and 7-CH_2), 1.7–1.8 (4H, m, 5- and 6-CH_2), 5.2 (1H, m, $CO_2CH(CH_3)_2$), 1.3 (6H, d, $CO_2CH(CH_3)_2$), 5.5 (2H, broad s, NH_2, disappears on addition of D_2O).

3.1.5. 2-Amino-3-butoxycarbonyl-4,5-tetramethylenethiophene

A mixture of 2-amino-3-ethoxycarbonyl-4,5-tetramethylenethiophene[12,13] (7.94 g, 0.035 mol) and butan-1-ol (160 ml) was stirred under a nitrogen atmosphere, and titanium isopropoxide (98%, 6.82 g, 0.023 mol) was added. After stirring and refluxing under nitrogen for 40 h, the solvent was removed by rotary evaporation from the clear yellow liquid. Water was added to the residual syrup, which solidified and was collected as a light buff powder (10.69 g). Hot filtration and recrystallisation (100–120° ligroin) gave translucent pale yellow chunky crystals (5.70 g, 64% purified yield, m.p. 41.5–43°C). Microanalysis found C, 61.7; H, 7.6; N, 5.75; S, 12.7% ($C_{13}H_{19}NO_2S$ requires C, 61.6; H, 7.6; N, 5.5; S, 12.7%). FTIR (KBr)/cm^{-1}: 3427, 3323 (NH); 1666, 1651 (C=O, NH).

3.1.6. 2-Acetylamino-3-butoxycarbonyl-4,5-tetramethylenethiophene

A mixture of butan-1-ol (40 ml) and 2-acetylamino-3-carboxyethyl-4,5-tetramethylenethiophene[13,29] (1.00 g, 3.7 mmol) was stirred under nitrogen at room temperature, titanium isopropoxide (97%, 0.66 g, 2.2 mmol) introduced and then refluxed under nitrogen with stirring for 24 h. The clear

liquor was rotary evaporated to dryness and the buff residue stirred with a mix of HCl (36%, 5 ml) and water (45 ml) before filtering. The solid was washed neutral and air-dried to give a light buff powder (1.20 g, m.p. 74–78°C). Recrystallisation (100–120° ligroin) yielded white needles (0.78 g, 71% purified yield, m.p. 76–77°C). Microanalysis found C, 60.7; H, 7.05; N, 4.65; S, 11.0% ($C_{15}H_{21}NO_3S$ requires C, 61.0; H, 7.2; N, 4.7; S, 10.9%). FTIR (KBr)/cm^{-1}: 3265 (NH); 1690, 1681, 1657 (C=O, NH).

3.1.7. 2-Amino-3-cyano-4,5-hexamethylenethiophene

Cyclooctanone (98%, 9.66 g, 0.075 mol), acetic acid (99%, 2.0 ml), ammonium acetate (1.0 g), malononitrile (99%, 5.51 g, 0.083 mol) and toluene (30 ml) were refluxed with stirring under a Dean-Stark trap for 4 h, adding further acid (1.6 ml) after 1 h. The yellow–orange liquid was washed several times with water, dried over magnesium sulphate and rotary evaporated to give crude cyclooctylidenemalononitrile. To this, ethanol (30 ml) and sulphur (2.40 g, 0.075 mol) were added, followed by treatment with morpholine (7.5 ml) in one portion and heating to reflux with stirring for 45 min. Rotary evaporation produced a brown oil, which solidified on stirring into water. Filtering and water-washing gave a light reddish-brown powder (14.50 g, 94% crude yield based on ketone, m.p. 97.5–104°C). Three recrystallisations (ligroin) gave yellow, analytically pure crystals of m.p. 105–106°C, lit.[23] 108°C, lit.[25] 98–102°C. Microanalysis found C, 64.1; H, 6.85; N, 13.55; S, 15.3% ($C_{11}H_{14}NS$ requires C, 64.0; H, 6.8; N, 13.6; S, 15.5%). IR (nujol)/cm^{-1}: 3430, 3330, 3220 (NH_2), 2200 (C≡N).

3.1.8. 2-Amino-3-methoxycarbonyl-5-methylthiophene

A stirred mixture of methyl cyanoacetate (99%, 20.02 g, 0.20 mol), sulphur (7.05 g, 0.22 mol), triethylamine (16 ml) and DMF (60 ml) was heated to 45–50°C and propanal (97%, 11.97 g, 0.20 mol) in ethanol (10 ml) was added dropwise at this temperature over half an hour. After stirring for 1 h at 50–56°C, the liquor was stirred into water (400 ml) causing rapid separation of solid. This material was filtered off after standing overnight giving a pink–red powder (29.60 g, 86% crude yield, m.p. 111–115°C), which was thoroughly water-washed. Two recrystallisations from methanol (*ca* 2 ml g^{-1}, charcoal) produced pale yellow crystals (m.p. 117–118°C). Microanalysis found C, 49.3; H, 5.25; N, 8.2; S, 18.6% ($C_7H_9NO_2S$ requires C, 49.1; H, 5.3; N, 8.2; S, 18.7%). FTIR (KBr)/cm^{-1}: 3414, 3292 (NH); 1667 (C=O).

3.1.9. 2-Amino-3-methoxycarbonyl-5-phenylthiophene

A stirred mixture of methyl cyanoacetate (99%, 10.01 g, 0.10 mol), sulphur (3.53 g, 0.11 mol), DMF (30 ml) and triethylamine (8 ml) was treated dropwise at 48–55°C with phenylacetaldehyde (90%, 11.40 g, 0.09 mol) in ethanol

(20 ml) over 30 min. A little pale yellow solid precipitated towards the end of the addition; the suspension was stirred for 1 h at 45–55°C and left to stand overnight. The solid was collected and washed with ice-cold ethanol (10 ml) to give a cream crystalline powder (8.34 g, 40% crude yield based on phenylacetaldehyde, m.p. 180–185°C). Recrystallisation (methanol/DMF 4:1), with hot filtration to remove residual sulphur, followed by two further recrystallisations (ethyl acetate/100–120° ligroin), gave analytically pure, shiny white rods of m.p. 188°C. Microanalysis found C, 61.8; H, 5.0; N, 6.05; S, 13.9% ($C_{12}H_{11}NO_2S$ requires C, 61.8; H, 4.75; N, 6.0; S, 13.7%). FTIR (KBr)/cm^{-1}: 3465, 3353 (NH); 1671 (C=O).

3.1.10. 5-Acetyl-2-amino-3-methoxycarbonyl-4-methylthiophene
Morpholine (10 ml) was added at 55°C to a stirred mixture of acetylacetone (98%, 10.22 g, 0.10 mol), methyl cyanoacetate (99%, 10.01 g, 0.10 mol), sulphur (3.21 g, 0.10 mol) and ethanol (20 ml), turning it deep yellow–orange. The mixture was stirred at 70°C for 1 h, most of the sulphur dissolving after 15 min, and cooled in ice before a few lumps of ice were added to induce crystallisation. After standing in ice for a few hours, the brown solid was collected, washed with ethanol and then with water to give a sandy-coloured solid (9.44 g, 44% crude yield), which was recrystallised (methanol) yielding shiny beige leaflets (m.p. 160–161°C, lit.[12] 31% yield, m.p. 161°C).

3.1.11. 2-Amino-5-cyano-3-ethoxycarbonyl-4-methylthiophene
To a mixture of 3-aminocrotononitrile (96%, 8.55 g, 0.10 mol), ethyl cyanoacetate (98%, 11.54 g, 0.10 mol), sulphur (3.21 g, 0.10 mol) and ethanol (20 ml) at 50°C was added diethylamine (10 ml). The mixture was stirred at 70°C for 5.5 h, diluted with a little water and placed in a refrigerator overnight. Filtration, followed by ethanol- and water-washing, gave a khaki-coloured material (3.92 g, 19% crude yield). Recrystallisation (2-ethoxyethanol twice, toluene, 2-ethoxyethanol twice) yielded analytically pure, translucent beige crystals, m.p. 200–201°C. Microanalysis found C, 51.3; H, 4.7; N, 13.1; S, 15.2% ($C_9H_{10}N_2O_2S$ requires C, 51.4; H, 4.8; N, 13.3; S, 15.25%). DSC suggested purity, showing a sharp endotherm at 201.8°C. FTIR (KBr)/cm^{-1}: 3393, 3294, 3258 (NH); 2204 (C≡N); 1674 (C=O). PMR (DMSO-d_6): 8.08 (2H, s, NH_2), 4.17 (2H, q, $CO_2CH_2CH_3$), 1.25 (3H, t, $CO_2CH_2CH_3$), 2.33 (3H, s, CH_3).

3.2. Preparation of dyes

The methods of synthesis and purification for each dye are listed in Table 3; the preparation of the dyes of type (**1**; 4,5-$(CH_2)_4$-) and (**1**; 4-CH_2CO_2Et) has already been described.[20]

3.2.1. Diazotisation methods

The presence of an excess of nitrous acid was tested for (after dilution of the sample if necessary) by starch–iodide paper; confirmation of the presence of diazonium ions was made by the formation of an intense coloration on addition of a sample to a solution of *N*-1-naphthylethylenediamine hydrochloride.

The following methods of diazotisation were used:

A. The amine was dissolved by warming in aqueous HCl (17%, 2.0 ml per mmol amine). Sodium nitrite (5–10% excess) in water (0.4 ml per mmol amine) was added over 30 min at 0–5°C and the whole stirred at this temperature for 30–60 min.
B. As in A, except aqueous HCl (17%, 3.0 ml per mmol amine) was used.
C. As in A, except aqueous HCl (18%, 1.5 ml per mmol amine) and acetone (0.5 ml per mmol amine) was used.
D. The amine was dissolved by warming in aqueous HCl (35%, 2.3 ml per mmol amine) and water (1.5 ml per mmol amine). Ice (5 g per mmol amine) and water (5 ml per mmol amine) were added in one portion followed by sodium nitrite (4% excess) in water (0.5 ml per mmol amine) having ensured that the first addition lowered the mixture temperature below 5°C. The whole was stirred for 15 min at 0°C.
E. The amine was dissolved by warming it in aqueous sulphuric acid (35%, 3.9 ml per mmol amine). Sodium nitrite (5–10% excess) in water (1.0 ml per mmol amine) was added over 30 min at 0–5°C and the whole stirred at this temperature for 60 min.
F. As in E, except aqueous sulphuric acid (54%, 3.4 ml per mmol amine) was used.
G. Nitrosylsulphuric acid was prepared by adding sodium nitrite (10% excess) to sulphuric acid (98%, 0.4 ml per mmol amine) at 20–30°C, heating to 60–65°C over 10 min with stirring and maintaining this temperature for up to 5 min to ensure complete dissolution. After allowing the solution to cool, a mixture of acetic and propionic acids (5:1, 0.64 ml per mmol amine) was added at below 30°C. The amine was added over 20–30 min below 5°C and the whole stirred at 0–5°C for 2–4 h.

3.2.2. Coupling methods

Sulphamic acid was added to the coupler solution before addition of the diazonium mixture if it had not been already added at the end of the diazotisation.

For dyes derived using diazotisation methods A–C, the coupler was dispersed in a mixture of acetic acid (99%, 0.25 ml per mmol amine), water

TABLE 3
Synthesis and Purification of the Dyes **1**

Substituents			Method/ molarity	Crude yield (g/%)	Purification method	Pure yield (g/%)	%s	Appearance	m.p. (°C)
3	4	5							
CN	-$(CH_2)_3$-		B/10	2.08/64	Δρρβ	0.25/8	12	bronze crystalline powder	185–186
CO_2Me	-$(CH_2)_3$-		D/20	5.44/69	Γηηλλ	0.23/3	6/4	red fibrous solid	163.5–165
CO_2Et	-$(CH_2)_3$-		D/20	4.97/61	Παααμα	0.29/4	6	shiny dark red crystals	139–140
CN	-$(CH_2)_5$-		E/10	2.88/73	Δμρ	0.88/22	31	red–purple blocks	166–167
CO_2Me	-$(CH_2)_5$-		C/7.5	2.20/.74	Παα	0.30/10	14	red needles	127–128
CO_2Et	-$(CH_2)_5$-		C/10	2.92/83	Παανν	0.45/13	15	bright red solid	135.5–136.5
CN	-$(CH_2)_6$-		E/10	4.02/99	Δββ	1.16/29	46/46	purple crystalline solid	155.5–156.5
CN	-$(CH_2)_{10}$-		F/8.0	3.19/86	Δαβ	1.05/28	33	red crystalline powder	160–160.5
CN	-PhC_2H_4-		F/8.0	2.40/71	Δγεεεμη	0.25/7	10	dark crystals	212–214
CN	-C_2H_4Ph-		F/8.0	2.67/79	Δρα	0.33/10	31/24	green crystalline powder	213–214
CN	Me	Me	E/10	3.15/90	Δδ	0.79/23	76/68	bronze and gold crystals	197-198
CO_2Me	Me	Me	D/10	2.14/56	Δνν	0.38/10	18	red fibrous needles	135–136
CO_2Et	Me	Me	A/10	-/-	Πα	0.30/8	—	red–purple crystals	123–124
CO_2Me	H	Me	E/10	1.58/43	Πββ	0.43/12	28	shiny purple–red leaflets	138.5–139
CO_2Me	H	Et	E/10	-/-	Πα	0.90/23	—	red needle-like crystals	107–107.5
CO_2Me	H	Bu^n	E/10	-/-	Πθθ	0.72/17	—	red–violet crystalline solid	76–76.5
CO_2Me	H	Ph	G/5.0	1.63/75	Θ ββ	0.26/12	16	red solid	141.5–142
CO_2Me	H	Ac	G/5.0	1.60/80	Λμ	0.46/23	46/37	fine purple needles	174.5–175
CO_2Me	Me	Ac	G/5.0	1.58/77	Λμεε	0.31/15	67/52	fine crimson needles	157–158
CO_2Et	Me	CN	G/5.0	1.78/87	μμμμημπ	0.95/46	53	shiny green crystals	203–204
CN	Me	CN	G/5.0	1.60/88	Λμεμδμ	0.35/19	22	shiny green needles	226–228
$CONH_2$	H	Ph	G/10	3.53/84	μμμμμμ	0.75/18	38/32	dark crystalline powder	189–189.5

Method—diazotisation procedure (see Section 3.2.1); molarity—amount of amine used in mmol.
Purification method—column chromatography: Γ (silica/toluene), Δ (silica/toluene:ethyl acetate 95:5), Θ (as in Δ, except ratio gradually changed to 90:10), Λ (as in Δ, except ratio 85:15), Π (as in Δ, except alumina). Recrystallisation: α (ethanol), β (aqueous ethanol), γ (ethanol/DMF), δ (2-ethoxyethanol), ε (aqueous 2-ethoxyethanol), η (aqueous 2-methoxyethanol), θ (methanol), λ (methanol/DMF), μ (toluene), ν (toluene/60–80° ligroin), π (toluene/80–100° ligroin), ρ (toluene/100–120° ligroin).
%s—Percentage yield of purification process, i.e. the percentage amount of pure dye obtained from the crude dye used in the purification (a second figure represents the theoretical pure yield, i.e. the percentage amount of pure dye obtained if all the crude sample had been used in the purification process, extrapolated from the percentage yield of the purification process).

(0.5 ml per mmol amine) and sodium acetate (0.5 g per mmol amine), the mixture cooled below 5°C and the diazonium solution added below this temperature over 5–10 min. After stirring at 0–5°C for 2–4 h or overnight, the mixture was diluted, filtered and water-washed neutral.

For method D, aqueous acetone was used,[21] whereas with methods E–G, a mixture of coupling component, water (4.9 ml per mmol amine), HCl (36%, 0.10 ml per mmol amine) and ice (5 g per mmol amine) was employed. Addition of the diazonium mixture was made at 0–5°C and the whole stirred for at least 2 h before diluting or raising the pH to 4.5 (aqueous NaOH or sodium acetate) prior to filtering and water-washing neutral.

The crude products were isolated as solids and purified by a combination of column chromatography and recrystallisation as detailed in Table 3. The purified dyes were all found to have satisfactory ($\leq \pm 0.3\%$) elemental analyses (C, H, N and S).

4. CONCLUSIONS

Diazo components produced directly from the Gewald reaction can be used to make yellow–red to violet disperse dyes. The amines possessed sufficiently different basicities to warrant the employment of various conditions for diazotisation. The direct method was suitable for derivatives lacking strong electron-withdrawing groups, although as the hydrophobicity of the amine increased, higher acidities were necessary; in certain cases, the required acidity had a deleterious effect on purity. Phenyl and strong electron-acceptor substituents reduced hydrophilicity and basicity, respectively, to the extent that nitrosylsulphuric acid was needed for satisfactory diazotisation; fortunately, these groups conferred improvements in stability. Consequently, the yields and purities of the more bathochromic members of the series tended to be higher.

General trends in the physical properties of the dyes could be identified and explained. Chemical shifts observed in the ^{13}C NMR spectra of the dyes were consistent with that reported for a carbocyclic analogue.

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